

Cost-effectiveness of vitamin D supplementation and exercise in preventing injurious falls among older home-dwelling women: findings from an RCT

R. Patil¹ · P. Kolu¹ · J. Raitanen^{1,2} · J. Valvanne^{3,4,5,6} · P. Kannus^{1,3,7} · S. Karinkanta¹ · H. Sievänen¹ · K. Uusi-Rasi^{1,8}

Received: 9 March 2015 / Accepted: 7 July 2015 / Published online: 24 July 2015
© International Osteoporosis Foundation and National Osteoporosis Foundation 2015

Abstract

Summary This study assessed the cost-effectiveness of vitamin D supplementation and exercise, separately and combined, in preventing medically attended injurious falls among older home-dwelling Finnish women. Given a willingness to pay of €3000 per injurious fall prevented, the exercise intervention had an 86 % probability of being cost-effective in this population.

Introduction The costs of falling in older persons are high, both to the individual and to society. Both vitamin D and exercise have been suggested to reduce the risk of falls. This study assessed the cost-effectiveness of vitamin D supplementation and exercise, separately and combined, in preventing medically attended injurious falls among older Finnish women.

Methods Economic evaluation was based on the results of a previously published 2-year randomized controlled trial (RCT) where 409 community-dwelling women aged 70 to 80 years were recruited into four groups: (1) no exercise + placebo (D-Ex-), (2) no exercise + vitamin D 800 IU/day (D+Ex-), (3) exercise + placebo (D-Ex+), and (4) exercise + vitamin D 800 IU/day (D+Ex+). The outcomes were medically attended injurious falls and fall-related health care utilization costs over the intervention period, the latter evaluated from a societal perspective based on 2011 unit costs. Incremental cost-effectiveness ratios (ICER) were calculated for the number of injurious falls per person-year prevented and uncertainty estimated using bootstrapping.

Results Incidence rate ratios (95 % CI) for medically attended injurious falls were lower in both Ex+ groups compared with D-Ex-: 0.46 (0.22 to 0.95) for D-Ex+, 0.38 (0.17 to 0.81) for D+Ex+. Step-wise calculation of ICERs resulted in exclusion of D+Ex- as more expensive and less effective. Recalculated ICERs were €221 for D-Ex-, €708 for D-Ex+, and €3820 for D+Ex+; bootstrapping indicated 93 % probability that each injurious fall avoided by D-Ex+ per person year costs €708. At a willingness to pay €3000 per injurious fall prevented, there was an 85.6 % chance of the exercise intervention being cost-effective in this population.

Conclusions Exercise was effective in reducing fall-related injuries among community-dwelling older women at a moderate cost. Vitamin D supplementation had marginal additional benefit. The results provide a firm basis for initiating feasible and cost-effective exercise interventions in this population.

Keywords Cost-effectiveness · Elderly · Exercise · Injurious falls · Vitamin D

✉ R. Patil
radhika.patil@uta.fi

¹ The UKK Institute for Health Promotion Research, P.O. Box 30, 33501 Tampere, Finland
² School of Health Sciences, University of Tampere, Tampere, Finland
³ School of Medicine, University of Tampere, Tampere, Finland
⁴ Purchasing Committee for the Promotion of Senior Citizens' Welfare, Tampere, Finland
⁵ Gerontology Research Center, Universities of Jyväskylä and Tampere, Jyväskylä, Finland
⁶ Department of Internal and Respiratory Medicine, Tampere University Hospital, Tampere, Finland
⁷ Department of Trauma, Musculoskeletal Surgery and Rehabilitation, Tampere University Hospital, Tampere, Finland
⁸ Research Department, Tampere University Hospital, Tampere, Finland

Introduction

Falls and fall-related injuries among older people are a major public health concern causing significant morbidity and mortality. Approximately 30 % of community-dwelling people aged 65 years or older, and even 50 % of those 80 years or older, report having had a fall over the past year [1, 2]. The costs of falling are high, both to the individual and to society. A fifth of fall incidents require medical attention, and serious injuries occur with 10–15 % of falls, 5 % resulting in fractures, and 1–2 % in hip fractures [3, 4]. National fall-related costs of prevalence-based studies are between 0.85 and 1.50 % of the total health care expenditures, 0.07 % to 0.20 % of the gross domestic product in the USA, Australia, and the UK [5]. In Finland (current population 5.4 million), the costs of hospital inpatient care due to falls were close to €400 million in 2012 [6].

Although challenging, falls prevention is widely seen as the most essential element in planning effective injury and fracture prevention strategies for older adults, since a greater propensity to fall increases the risk of fracture and other injuries considerably [4, 7, 8]. Regular strength and balance training for community-dwelling older adults can reduce the risk of both noninjurious and injurious falls by 15–50 % [4, 9–11]. Not only individually tailored training but also more untargeted group exercise programs are effective in preventing falls [12, 13]. Vitamin D, in turn, is known to be vital for bone metabolism and has been suggested to reduce the risk of fractures [14]. In addition, low S-25-OHD levels are associated with falls [15, 16].

Evidence for the economic effectiveness of fall prevention in the elderly is growing, and various intervention programs have been deemed to be cost-effective [17–19]. Evidence concerning cost-effectiveness of vitamin D in falls prevention is sparse, although a meta-analysis showed that vitamin D supplementation reduced older adults' fall risk by more than 20 % compared with individuals receiving calcium or placebo [15]. In addition, in seven European countries, supplementation with calcium and vitamin D was cost-effective in preventing hip fractures among institutionalized elderly women [20]. For its safety, availability, and low costs, vitamin D supplementation has great potential for widespread implementation.

This study assessed the cost-effectiveness of vitamin D supplementation and exercise in preventing medically attended injurious falls, based on results from a four-armed RCT on falls prevention among older home-dwelling Finnish women [21]. Although the RCT examined the effectiveness of the interventions on preventing falls, effectiveness on fall-related health care utilization costs was not known. In this study, the four treatment arms (depending on whether or not participants received exercise and vitamin D) were compared for intervention costs as well as for differences in fall-related

health care utilization costs. Fall-related health care costs were evaluated over the 2-year intervention period from a societal perspective, based on 2011 unit costs. ICERs were calculated for the number of injurious falls per person-year prevented in each treatment arm.

Methods

The DEX RCT: study design, interventions, and outcomes

The cost-effectiveness analysis is based on data from the vitamin D and exercise for falls prevention trial (DEX), conducted in Finland from 2010 to 2013 (NCT00986466). The DEX study was a 2-year randomized, double-blind placebo-controlled vitamin D, and open exercise intervention trial where 409 community-dwelling, independently living Finnish women aged 70 to 80 years were randomized into one of four groups: (1) no exercise + placebo (D–Ex–), (2) no exercise + vitamin D 800 IU/day (D+Ex–), (3) exercise + placebo (D–Ex+), and (4) exercise + vitamin D 800 IU/day (D+Ex+). To be eligible, participants were required to have fallen at least once during the previous year, had no contraindications to exercise, and had less than 2 h of moderate to vigorous exercise per week. Participants received one daily pill containing either 800 IU (20 µg) vitamin D₃ or placebo for 24 months [22], and compliance was confirmed by pill counts. Exercise consisted of supervised group training classes two times a week for the first 12 months and once a week for the remaining 12 months. The training program was progressive and consisted of strength, balance, agility, and mobility training, as described in detail elsewhere [22]. Exercisers also had a home-training program modified from the supervised exercises, to be done on all rest days during the first year and at least three times a week in the second year. The exercise protocol was based on previously tested protocols for falls prevention [23, 24]. Participants in the nonexercising groups were asked to maintain their pre-study level of physical activity.

Participants recorded fall incidents in fall diaries returned monthly via postage-prepaid envelopes. Details of each registered fall were ascertained by telephone. All reported fall-related injuries (including bruises, abrasions, contusions, muscle or joint pain, head injuries and fractures) were recorded. A fall was defined as “an unexpected event in which the participants come to rest on the ground, floor or lower level” [25]. Medically attended fall injuries were defined according to medical care use and conformed to a definition recently recommended by Schwenk et al. and included injuries requiring medical/health professional examination, or emergency/inpatient treatment [26].

Effects of the RCT

The DEX RCT showed that while neither exercise nor vitamin D affected the rate of falls, the rate of medically attended injurious falls and injured fallers more than halved with exercise training. Incidence rate ratios (IRR; 95 % CI) for medically attended injurious falls were lower in both Ex+ groups compared with D–Ex– group: 0.46 (0.22 to 0.95) for the D–Ex+ group and 0.38 (0.17 to 0.81) for the D+Ex+ group. The D+Ex– group did not differ from D–Ex– group. Effects of the intervention are described in detail elsewhere [21]. The number of participants who needed to be treated with the exercise program (NNT) over 24 months to prevent one medically attended injurious fall event was calculated as the reciprocal of the absolute difference in the incidence between each of the intervention groups and the reference D–Ex– group.

Economic evaluation

Intervention costs included costs due to the exercise program as well as vitamin D supplementation. Exercise implementation included hourly supervisors' (physiotherapists) salaries including administrative costs, material costs, and overheads calculated for the recommended exercise dose over the intervention period (twice a week for 12 months and once a week for the subsequent 12 months). We focused on implementation costs only; although there were costs associated with developing and evaluating the program, these were incurred before the trial and were not incremental to this program. Research protocol costs were, therefore, excluded. Vitamin D supplement costs (Oy Verman Ab, Kerava, Finland) were based on pharmacy prices. Average intervention costs per participant were calculated assuming all participants randomized to the exercise groups attended all of the offered training sessions, and those randomized to vitamin D supplementation had 100 % pill compliance over the entire 2-year intervention period.

The Pegasos patient medical records of the City of Tampere and the Tampere University Hospital were searched for fall-related health services utilization for all injurious falls reported during the intervention period. The use of these centralized data records ensured that all fall-related public health service utilization was taken into account. Records were checked specifically for visits around the date on which each medically treated injurious fall occurred (data from falls diaries, confirmed over telephone interview). Treatments mentioning “fall,” “fall-related,” or “fall injury” as diagnosis criteria or history were recorded. Follow-up visits were scrutinized for as long as the original fall was mentioned in the history or diagnosis. All visits to outpatient health care (nurse and specialist consultations), telephone consultations, emergency department visits, ambulance services, operations or treatments according to ICD-10 diagnosis codes, related inpatient

hospital days, and social services (home-care) utilization for each reported injurious fall were scrutinized. Visits to private health care providers were estimated based on self-report by the participants.

Outpatient visits were matched with appropriate unit costs published by the Finnish National Institute for Health and Welfare [27]. Inpatient unit costs were based on detailed “Diagnosis Related Group” information according to ICD-10 diagnoses and procedure codes [27, 28]. Procedure unit costs included a standard number of inpatient days, depending on the type of procedure/surgery and duration of rehabilitation.

Costs were reported based on the tax-based health care system of Finland and evaluated from a societal perspective including fall-related health care costs for the municipality and costs borne by the patients. This was because in Finland, the patients' municipality of residence reimburses real health care costs to the relevant hospital district. Daily charges for outpatient and inpatient care also create a small cost to the patient. Unit costs were entered at the price level for 2011 in euros (€) [27] and included salary costs, administrative and laboratory expenses, equipment and medication costs, and costs for all professionals participating in the provision of health care. Costs borne by the patients themselves were included in the unit costs for outpatient health care, while those for inpatient care were added separately (approximately 5 %) as recommended [27]. Because the travel expenses and time costs related to the use of health services were not known, they were not included in the calculation. Also, prescription medication costs were not included since it was not possible to distinguish fall-related prescriptions from other commonly used medications, especially in this age group with comorbidities.

Statistical methods

Descriptive information and differences in costs between groups are reported as arithmetic means and standard deviations (SD). Between-group differences in costs were tested with the nonparametric Kruskal-Wallis tests and significance values calculated with bootstrap methods. Results were considered to be statistically significant if $p < 0.05$. Cost-effectiveness is expressed in terms of the incremental cost-effectiveness ratios (ICER), calculated as the ratio of the difference in mean total costs and mean effects at the group level. Total costs included fall-related health care costs and intervention costs. Standardized measures of *injurious falls per person year* and *fall-related costs per person year* were used, since they took into account the variable follow-up times for individuals in the trial [29]. The total cost of intervention over 2 years was used for the calculations, since this provided a conservative estimate of the actual expenditure regardless of compliance. The control D–Ex– group represented the alternative of “usual care” and had the same ICER as its average cost-effectiveness ratio (ratio of mean

total cost and mean effect). Alternative interventions were ranked according to their effectiveness, and ICERs were calculated [30]. Using the principle of extended dominance, alternative interventions that were more expensive and less effective than usual care were excluded, and ICERs were recalculated for the remaining interventions [30, 31]. Uncertainty around the ratios was estimated using bootstrapping with 5000 iterations to generate 95 % confidence ellipses for the joint distribution of cost and effectiveness outcomes, graphically represented on a cost-effectiveness plane. Cost-effectiveness acceptability curves (CEAC) were presented to indicate the probability of any of the alternative interventions' being cost-effective. To evaluate the robustness of the findings, we performed sensitivity analysis, using doubled intervention costs. Also, we combined the groups according to whether they received the exercise intervention or not, and exercisers were compared with nonexercisers regardless of vitamin D supplementation. Corresponding ICERs and CEACs were also reported. All analyses were conducted using Stata statistics software version 12.1.

Results

Effects

There were no clinically relevant between-group differences in age or anthropometry at baseline (Table 1). Thirty-nine women (9.5 %) did not complete the end point measurements, most of them due to health reasons, and four died. Mean pill compliance (range) was 98 % (42 to 100 %), while mean exercise compliance measured as attendance at all offered training sessions for group and home training was 73 % (0 to 97 %) and 66 % (0 to 100 %), respectively. At the end of the intervention, there was no interaction between vitamin D and exercise [21]. Table 1 shows the effect of interventions on all falls and medically attended injurious falls as well as the numbers needed to treat (NNT) over 24 months to prevent one medically attended injurious fall. In total, there were 72 medically attended injurious falls and 57 medically attended injured fallers. Table 1 also lists the medically attended fall injuries by group over 24 months (categorized as the more severe injury in cases where more than one injury was reported per fall).

Costs

Table 2 shows group differences in mean costs for health care services utilization as well as average intervention costs. The average 2-year cost of vitamin D supplementation was €73 per participant (€0.10 per pill), while that of implementing the exercise intervention was €47 per participant (€63 per hour). There were no significance between group differences for

mean fall-related health care costs (Table 2). Total costs per person year (including costs of the 2-year intervention) were lowest in the D–Ex– group €30.9 (9.5), compared with €73.4 (10.4) in D–Ex+, €188.0 (45.4) in D+Ex+, and €206.9 (80.2) in D+Ex– (Table 3).

Cost-effectiveness

ICERs calculated for alternative interventions ranked according to their effectiveness are shown in Table 3. In the first step, the D+Ex– group was excluded since it was followed by an intervention that was both more effective and less expensive. Recalculation for the remaining groups resulted in an ICER of €221 for group D–Ex–, €708 for group D–Ex+ and €3820 for group D+Ex+. Figure 1 shows the cost-effectiveness plane and cost-effectiveness acceptability curve (CEAC) for D–Ex+ compared with D–Ex– for the outcome “medically-attended injurious falls per person year”; 93.2 % of bootstrap pairs were in the north-east quadrant indicating that the intervention was more effective and more expensive for injurious falls prevented than usual care. In other words, the study indicated 93.2 % probability that each injurious fall avoided by group D–Ex+ per person year required an additional cost of €708. In Fig. 1, the CEAC cuts the *y*-axis at 0, showing that none of the joint density involves cost-savings. At a willingness to pay €3000 per injurious fall prevented, there was an 85.6 % chance of the exercise intervention being cost-effective in this population.

The corresponding ICERs per fall prevented (i.e., total number of falls in the comparator group minus total number of falls in the intervention group) were €250 for group D–Ex+ and €3920 for group D+Ex+.

Sensitivity analyses

The sensitivity analyses applied the assumption that the intervention costs would be two times higher (€146 for vitamin D and €94 for exercise). The results were quite similar to those in the basic analyses; D+Ex– was eliminated and recalculated ICERs were €1492 for group D–Ex+ and €6253 for group D+Ex+. The cost-effectiveness plane showed 93.3 % of bootstrap pairs in the north-east quadrant. Table 3 shows the ICERs for the combined exercise groups compared with no exercise. The combined exercise group was significantly more effective in reducing injurious falls. In the cost-effectiveness plane (Fig. 1), the cost-effect pairs were within the north-east and south-east quadrants, clustering around the *x*-axis indicating neither large nor significant differences in costs. The CEAC did not cut the *y*-axis at 0, indicating that about a third of the joint density (35.9 %) involved cost-savings. The probability of the exercise intervention being cost-effective was 95 % at a willingness to pay of €2240, based on available evidence.

Table 1 Baseline descriptive characteristics of the study groups, mean (SD), medically attended fall injuries over 24 months, and effects of interventions on all falls and medically attended injurious falls over 24 months

	D-Ex-	D+Ex-	D-Ex+	D+Ex+
Baseline characteristics	<i>N</i> =102	<i>N</i> =102	<i>N</i> =103	<i>N</i> =102
Age, year	73.8 (3.1)	74.1 (3.0)	74.8 (2.9)	74.1 (2.9)
Height, cm	160.7 (5.4)	159.2 (5.8)	159.4 (6.1)	159.7 (5.9)
Weight, kg	72.0 (12.4)	73.0 (13.1)	70.9 (10.6)	73.2 (10.5)
S-25(OH)D, nmol/L	67.6 (18.8)	65.8 (17.1)	69.5 (18.0)	65.5 (17.5)
Daily steps, first month	6000 (2636)	5812 (2842)	5920 (2458)	5831 (2504)
MMSE score (range 0–30)	28.5 (1.7)	28.3 (1.4)	28.2 (1.4)	28.3 (1.5)
SPPB score (range 0–12)	10.6 (3–12)	10.7 (1–12)	10.9 (7–12)	10.8 (5–12)
Number of diagnosed diseases	2.2 (1.3)	2.3 (1.3)	2.0 (1.4)	2.3 (1.3)
Number of medications	2.5 (2.0)	2.6 (1.9)	2.3 (2.0)	2.7 (1.9)
Medically attended fall injuries, <i>n</i>	<i>N</i> =102	<i>N</i> =96	<i>N</i> =99	<i>N</i> =100
Fractures	6	6	5	3
Head/facial injuries	6	6	4	2
Other (abrasions, bruises, contusions)	16	8	5	5
Effects of intervention at 24 months				
All falls, <i>n</i>	229	228	241	230
Falls per person year	1.18 (1.6)	1.39 (2.1)	1.25 (1.6)	1.15 (1.2)
Injurious falls, <i>n</i>	28	20	14	10
Injurious falls per person year	0.14(0.3)	0.13(0.4)	0.08 (0.2)	0.05 (0.2)
NNT	Reference	16	8	6

MMSE mini-mental state examination, SPPB short physical performance test battery, NNT number needed to treat for 24 months to prevent one medically attended injurious fall, D-Ex- placebo and no exercise, D+Ex- vitamin D and no exercise, D-Ex+ placebo and exercise, D+Ex+ vitamin D and exercise

Discussion

Exercise was more effective than usual care in reducing injurious falls requiring medical care among 70–80-year-old community-dwelling women. This exercise intervention can be termed cost-effective from the Finnish societal perspective because it gave an additional benefit worth the additional cost [32]. In fact, the nature of the CEAC involves including the joint density of cost-effect pairs that falls in the north-east quadrant (more costly, more effective) as *cost-effective*, as the value of the willingness to trade between cost and effect increases [33]. Our study showed that with a willingness to pay of €3000 per injurious fall prevented, there was an 85.6 % chance of the exercise intervention being cost-effective in this population. Exercise combined with vitamin D had a relatively small increase in effect, while total costs were substantially more. Of note, exercise alone also improved physical functioning and may be effective in the long-term in saving on further costs of fall-related outpatient and inpatient visits.

Evidence for the economic effectiveness of fall prevention in the elderly is growing, and various intervention programs have been deemed to be cost-effective [17, 19]. A systematic review of economic evaluations of falls prevention interventions (eight studies that reported incremental cost per fall prevented) concluded that cost-effective interventions included strength and balance retraining, cataract surgery, and home

safety interventions [18]. Of three studies applying falls prevented as a measure of effectiveness, two proved the interventions to be cost-effective [34, 35], while one could show this only for participants with previous falls [36]. Two studies have shown that a multifactorial approach to fall prevention reduced neither the fall rate nor the costs among high-risk patients and were not superior to usual care in terms of utility (quality of life) [37, 38]. Multifactorial programs may also increase intervention costs substantially. Among exercise interventions, the most favorable incremental and widely applicable cost-effectiveness ratio was for the Otago Exercise Program [39]. A randomized controlled exercise trial on fracture risk, coronary heart disease, and health care costs in community-dwelling elderly women demonstrated a trend toward lower health care costs in the exercise group [40]. Another recent study estimated that a multimedia patient education program with health professional follow-up had a 52 % probability of being both more effective and less costly than usual care for the incremental cost per faller or per fall prevented [41]. A majority of studies have assessed only one component of a multifactorial approach to fall prevention, disregarding components that did not prove effective in preventing falls [36, 42]. Davis et al. [43] found that both once and twice weekly resistance training resulted in lower healthcare costs and was more effective than twice-weekly balance and tone classes, though the former excluded an

Table 2 Mean (SD) fall-related health care and intervention costs by group

Resource	Unit cost, €	D-Ex- (n=102)		D+Ex- (n=96)		D-Ex+ (n=99)		D+Ex+ (n=100)		p ^a
		Number of units	Mean costs (€)	Number of units	Mean costs (€)	Number of units	Mean costs (€)	Number of units	Mean costs (€)	
Primary health care										
Physician	96–110/visit	35	34.9 (124)	32	33.9 (131.9)	15	15.1 (54.8)	8	8.1 (44.7)	0.77
Nurse	34–48/visit	22	7.5 (22.4)	15	5.3 (15.1)	13	5.3 (38.1)	11	4.3 (23.8)	0.66
Other health professional	46/visit	3	1.4 (7.8)	2	1.0 (9.4)	3	1.4 (10.3)	1	0.5 (4.6)	0.86
Telephone consultation: Physician	23–26/call	6	1.5 (8.7)	3	0.8 (4.5)	0	0	2	0.5 (4.6)	0.71
Telephone consultation: Nurse	10/call	5	0.5 (2.2)	5	0.5 (5.1)	2	0.2 (1.4)	1	0.1 (1.0)	0.64
Specialist consultation	35/call	0	0	1	0.4 (3.6)	2	0.7 (7.0)	0	0	0.93
Secondary health care										
Ambulance call out	112/trip	1	1.1 (11.1)	1	1.2 (11.4)	3	3.4 (19.3)	0	0	0.65
Emergency department	347/visit	1	3.4 (34.4)	1	3.6 (35.4)	2	7.0 (49.1)	1	3.5 (34.7)	0.94
Outpatient department	290/visit	0	0	1	3.0 (29.6)	2	5.9 (58.3)	0	0	0.93
Hospitalization	1929–7258/hospitalization	0	0	5	196.1 (1352.0)	0	0	3	86.5 (609.2)	0.70
Personal social services										
Home care	42/visit	0	0	0	0	0	0	61	25.6 (256.2)	0.72
House call by nurse	61–110/visit	0	0	2	1.8 (17.4)	0	0	0	0	0.74
Physiotherapy services										
Outpatient visit (31–60 min)	115/visit	9	10.1 (58.6)	14	16.7 (115.6)	5	5.8 (41.5)	0	0	0.78
House call	215/visit	0	0	0	0	0	0	1	2.2 (21.5)	0.72
Telephone consultation	47/call	0	0	0	0	1	0.5 (4.7)	0	0	0.74
Private health care										
Physician	47–82/visit	1	0.8 (8.1)	0	0	2	1.3 (9.5)	0	0	0.66
Radiological investigations	81–84/x-ray	1	0.8 (8.0)	0	0	1	0.8 (8.4)	0	0	0.93
Total health care costs			61.9 (190.8)		264.3(1572.5)		47.4 (186.7)		131.2 (880.6)	
Intervention										
Exercise	63/hour		–		–		47		47	
Vitamin D (20 µg/day)	0.10/pill		–		73		–		73	

Unit costs estimated at the price level for 2011, in euros (€) [27]

D-Ex- placebo and no exercise, D+Ex- vitamin D and no exercise, D-Ex+ placebo and exercise, D+Ex+ vitamin D and exercise

^a Kruskal-Wallis test, significance values calculated with bootstrapping methods

outlier with multiple falls. Other studies substantially differ from our study methodologically, including various follow-up periods, different outcome measures, unequal cost compositions, and most importantly, various intervention approaches, making comparisons difficult [44]. Overall, the best value for money seems to come from single factor interventions such as home-based exercise programs targeted at high-risk groups [18].

In our study, average fall-related health care utilization costs were lowest in the group receiving the exercise intervention only, indicating that exercise may be effective in reducing fall-related medical costs. On the other hand, both groups receiving vitamin D supplementation (with or without exercise) showed higher medical costs. Two hip fractures (one of the most expensive fractures) occurred during the intervention period, both in women belonging to the D+Ex- group. One woman from the D+Ex+ group sustained a

vertebral fracture (requiring 3 U of hospitalization and 61 U of home care) and was responsible for a sizable proportion of the average medical unit costs associated with the group. Also, it is worth noting that although the control group had a greater number of injurious falls requiring medical care, these were treated on an outpatient basis and none required hospitalization. As a result, fall-related health care costs remained low in this group.

Our study has certain limitations. The trial primarily aimed to evaluate the effectiveness of the interventions in preventing falls and injuries among older home-dwelling women, and the power calculation was based on a reduction in the total number of falls, rather than costs. Severe fall-related injuries that result in higher health care costs are rare, and group differences are easily skewed by outlier values. Costs were calculated by scrutinizing register data of those who reported seeking medical treatment due to a fall. Although falls reported through falls

Table 3 Mean total costs (health care and intervention) and injurious falls per person year (SD) and incremental cost-effectiveness ratios (ICER)

Group	Sample size	Costs per person year in € (<i>C</i>)	Effects: injurious falls per person year (<i>E</i>)	Incremental cost (ΔC)	Incremental effect (ΔE)	ICER ($\Delta C/\Delta E$)
All intervention groups						
D-Ex-	102	30.9 (95)	0.14 (0.32)	30.9	0.14	220.7
D+Ex-	96	206.9 (786)	0.13 (0.38)	176.0	0.01	17,600
D-Ex+	99	73.4 (104)	0.08 (0.24)	-133.5	0.05	-2670
D+Ex+	100	188.0 (454)	0.05 (0.19)	114.6	0.03	3820
Cost-effectiveness results after excluding the intervention that is both more expensive and less effective than its successor						
D-Ex-	102	30.9 (95)	0.14 (0.32)	30.9	0.14	220.7
D-Ex+	99	73.4 (104)	0.08 (0.24)	42.5	0.06	708.3
D+Ex+	100	188.0 (454)	0.05 (0.19)	114.6	0.03	3820
Groups aggregated according to allocation to exercise						
No exercise (D-Ex- and D+Ex-)	198	80.9 (553)	0.13 (0.35)	80.9	0.13	622.3
Exercise (D-Ex+ and D+Ex+)	199	94.3 (330)	0.06 (0.22)	13.4	0.07	191.4

For reference groups (D-Ex- and no exercise), $\Delta C=C$, $\Delta E=E$ and $ICER=C/E$. Unit costs entered at the price level for 2011 [27]

D-Ex- placebo and no exercise, D+Ex- vitamin D and no exercise, D-Ex+ placebo and exercise, D+Ex+ vitamin D and exercise

diaries (returned monthly by mail) were ascertained for details of treatment with minimal delay to avoid recall bias, some of these may have been inadvertently missed or remained unreported. The present results are specific to the study interventions within this particular population of healthy vitamin D-

replete community-dwelling women who had fallen at least once in the previous year and may not be applicable to men, or to those in residential care. Also, since healthcare costs and content of usual care differ across countries, generalizing the results to other countries may not be relevant.

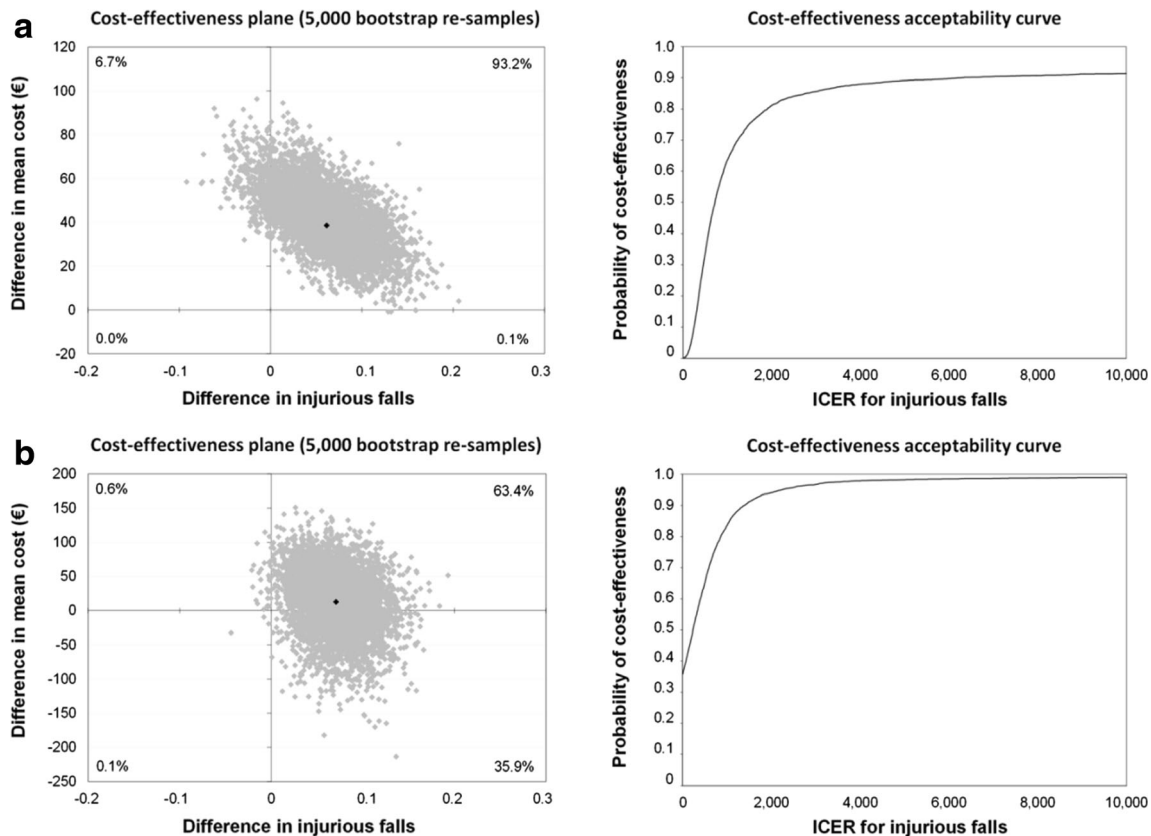


Fig. 1 Cost-effectiveness planes (5000 bootstrap resamples) (left) and acceptability curves (right) for injurious falls per person year: D-Ex+ compared with D-Ex- (a) and comparing combined exercise groups with no exercise groups (b)

This study also has several strengths. This economic evaluation was conducted alongside an RCT, with 2-year duration. To our knowledge, this is the first study examining cost-effectiveness of vitamin D supplementation in preventing injurious falls among community-dwelling older women. We evaluated cost-effectiveness of all the trial intervention arms using a step-wise approach to calculate ICERs, regardless of whether each intervention was effective in reducing falls or not [30]. Fall-related costs were specifically compared. Medical service utilization resulting from all reported falls was scrutinized through patient treatment records, which also included home care costs. Costs were calculated according to recently published unit costs for 2011 and represented average costs in Finland [27]. All analyses were based on the intention-to-treat principle, and there were no missing data to be accounted for, thus reducing uncertainty in estimation of the results. From the society's perspective, a favorable effect of exercise training on physical functioning (strength, balance, and mobility) may bring considerable additional cost savings in the long-term, as indicated by lower rates of injurious falls among previous exercisers [45]. Thus, total cost-effectiveness may be underestimated if only the intervention period is examined.

In conclusion, our strength and balance training was highly effective in reducing fall-related injuries among 70–80-year-old community-dwelling women at a moderate additional cost. The inclusion of vitamin D supplementation increased costs with marginal additional benefit. Because the training regimen is easily adoptable, a broad implementation of the program seems feasible. In other words, the results can be used as a firm basis to initiate cost-effective, feasible, and safe exercise programs for aging populations.

Acknowledgments The authors thank the Academy of Finland, the Competitive Research Fund of Pirkanmaa Hospital District, the Finnish Ministry of Education and Culture, the Juho Vainio Foundation, the National Doctoral Program of Musculoskeletal Disorders and Biomaterials (TBDP), the Finnish Cultural Foundation, the Tampere City Science Fund, and the Ella and Georg Ehmrooth Foundation for their financial support. The authors also wish to thank Dr. Esa Jämsen (M.D., PhD.) for technical advice and information on the Tampere City health services.

Conflicts of interest None.

Ethical approval All procedures performed in the study were in accordance with the ethical standards of the Pirkanmaa Hospital District Ethics Committee (R09090) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The trial is registered in the ClinicalTrials.gov register (NCT00986466). Permission for the use of patient data was obtained from the Department of the Social Services and Health Care, Tampere and the Pirkanmaa Hospital District Science Centre.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

- Hoidrup S, Sørensen T, Grønbæk M, Schroll M (2003) Incidence and characteristics of falls leading to hospital treatment: a one-year population surveillance study of the Danish population aged 45 years and over. *Scand J Public Health* 31:24
- Tinetti M, Williams C (1997) Falls, injuries due to falls, and the risk of admission to a nursing home. *N Engl J Med* 337:1279–1284
- Gillespie LD, Robertson MC, Gillespie WJ, Sherrington C, Gates S, Clemson LM, Lamb SE (2012) Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 9:CD007146
- Kannus P, Sievanen H, Palvanen M, Jarvinen T, Parkkari J (2005) Prevention of falls and consequent injuries in elderly people. *Lancet* 366:1885–1893
- Heinrich S, Rapp K, Rissmann U, Becker C, König H-H (2010) Cost of falls in old age: a systematic review. *Osteoporos Int* 21(6): 891–902
- National Institute for Health and Welfare, Finland (2014) Accidental falls and fall injuries in older people. *THL Injury Database 2015*: <http://www.thl.fi/en/web/injury-prevention/older-people>. Accessed 20 May 2015
- Korhonen N, Niemi S, Parkkari J, Sievänen H, Palvanen M, Kannus P (2013) Continuous decline in incidence of hip fracture: nationwide statistics from Finland between 1970 and 2010. *Osteoporos Int* 24:1599–1603
- Carter N, Kannus P, Khan K (2001) Exercise in the prevention of falls in older people: a systematic literature review examining the rationale and the evidence. *Sports Med* 31:427–438
- El-Khoury F, Cassou B, Charles M-A, Dargent-Molina P (2013) The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systematic review and meta-analysis of randomised controlled trials. *BMJ* 347:f6234
- Karinkanta S, Piirtola M, Sievänen H, Uusi-Rasi K, Kannus P (2010) Physical therapy approaches to reduce fall and fracture risk among older adults. *Nat Rev Endocrinol* 6:396–407
- Chang JT, Morton SC, Rubenstein LZ, Mojica WA, Maglione M, Suttrop MJ, Roth EA, Shekelle PG (2004) Interventions for the prevention of falls in older adults: systematic review and meta-analysis of randomised clinical trials. *BMJ* 328:680
- Skelton D, Dinan S, Campbell M, Rutherford O (2005) Tailored group exercise (Falls Management Exercise-FaME) reduces falls in community-dwelling older frequent fallers (an RCT). *Age Ageing* 34:636–639
- Barnett A, Smith B, Lord S, Williams M, Baumand A (2003) Community-based group exercise improves balance and reduces falls in at-risk older people: a randomised controlled trial. *Age Ageing* 32:407–414
- Bischoff-Ferrari H, Willett W, Wong J, Giovannucci E, Dietrich T, Dawson-Hughes B (2005) Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. *J Am Med Assoc* 293(18):2257–2264
- Bischoff-Ferrari H, Dawson-Hughes B, Willett W et al (2004) Effect of vitamin D on falls: a meta-analysis. *J Am Med Assoc* 291:1999–2006
- Dhesi J, Jackson S, Bearne L et al (2004) Vitamin D supplementation improves neuromuscular function in older people who fall. *Age Ageing* 33:589–595

17. Carande-Kulis V, Stevens JA, Florence CS, Beattie BL, Arias I (2015) A cost-benefit analysis of three older adult fall prevention interventions. *J Saf Res* 52:65–70
18. Davis J, Robertson M, Ashe M, Liu-Ambrose T, Khan K, Marra C (2010) Does a home-based strength and balance programme in people aged ≥ 80 years provide the best value for money to prevent falls? A systematic review of economic evaluations of falls prevention interventions. *Br J Sports Med* 44:80–89
19. Hektoen L, Aas E, Lurås H (2009) Cost-effectiveness in fall prevention for older women. *Scand J Public Health* 37:584–589
20. Lilliu H, Pamphile R, Chapuy M et al (2003) Calcium-vitamin D3 supplementation is cost-effective in hip fractures prevention. *Maturitas* 44:299–305
21. Uusi-Rasi K, Patil R, Karinkanta S, Kannus P, Tokola K, Lamberg-Allardt C, Sievänen H (2015) Exercise and vitamin D in falls prevention among older women: a randomized controlled trial. *JAMA Intern Med* 175(5):703–711
22. Uusi-Rasi K, Kannus P, Karinkanta S, Pasanen M, Patil R, Lamberg-Allardt C, Sievänen H (2012) Study protocol for prevention of falls: a randomized controlled trial of effects of vitamin D and exercise on falls prevention. *BMC Geriatr* 12:12
23. Sherrington C, Tiedemann A, Fairhall N, Close JC, Lord SR (2011) Exercise to prevent falls in older adults: an updated meta-analysis and best practice recommendations. *N S W Public Health Bull* 22:78–83
24. Karinkanta S, Heinonen A, Sievänen H, Uusi-Rasi K, Pasanen M, Ojala K, Fogelholm M, Kannus P (2007) A multi-component exercise regimen to prevent functional decline and bone fragility in home-dwelling elderly women: randomized, controlled trial. *Osteoporos Int* 18(4):453–462
25. Lamb SE, Jorstad-Stein E, Hauer K, Becker C (2005) Development of a common outcome data set for fall injury prevention trials: the Prevention of Falls Network Europe consensus. *J Am Geriatr Soc* 53:1618–1622
26. Schwenk M, Lauenroth A, Stock C, Moreno R, Oster P, McHugh G, Todd C, Hauer K (2012) Definitions and methods of measuring and reporting on injurious falls in randomised controlled fall prevention trials: a systematic review. *BMC Med Res Methodol* 12:50
27. Kapiainen S, Väisänen A, Haula T (2014) Terveysten- ja sosiaalihuollon yksikkökustannukset Suomessa vuonna 2011 [Health and social care unit costs in Finland 2011]. National Institute for Health and Welfare, Finland (in Finnish). THL Raportti 3
28. Nordiskt Center för patientgruppering and the Association of Finnish Local and Regional Authorities (AFLRA) (January 2011) NordDRG Users' Manual, Version 2011 FIN FULL PR1a: http://www.norddrg.net/norddrgmanual/NordDRG_2011_FIN/index.htm. Accessed 20 May 2015
29. Davis J, Robertson M, Comans T, Scuffham P (2011) Guidelines for conducting and reporting economic evaluation of fall prevention strategies. *Osteoporos Int* 22:2449–2459
30. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G (2005) Methods for the economic evaluation for health care programmes, 3rd edn. Oxford University Press, New York
31. Karlsson G, Johannesson M (1996) The decision rules of cost-effectiveness analysis. *Pharm Econ* 9(2):113–120
32. Doubilet P, Weinstein M, McNeil B (1986) Use and misuse of the term “cost-effective” in medicine. *N Engl J Med* 314(4):253–256
33. Fenwick E, O'Brien B, Briggs A (2004) Cost-effectiveness acceptability curves: facts, fallacies and frequently asked questions. *Health Econ* 13:405–415
34. Robertson M, Gardner M, Devlin N, McGee R, Campbell A (2001) Effectiveness and economic evaluation of a nurse delivered home exercise programme to prevent falls. 1: randomised controlled trial. *BMJ* 322:697–701
35. Rizzo J, Baker D, McAvay G, Tinetti M (1996) The cost-effectiveness of a multifactorial targeted prevention program for falls among community elderly persons. *Med Care* 34:954–969
36. Salkeld G, Cumming R, Thomas M, Szonyi G, Westbury C, O'Neill E (2000) The cost effectiveness of a home hazard reduction program to reduce falls among older persons. *Aust N Z J Public Health* 24(3):265–271
37. Peeters G, Heymans M, de Vries O, Bouter L, Lips P, van Tulder M (2011) Multifactorial evaluation and treatment of persons with a high risk of recurrent falling was not cost-effective. *Osteoporos Int* 22:2187–2196
38. Hendriks M, Evers S, Bleijlevens M, van Haastregt J, Crebolder H, van Eijk J (2008) Cost-effectiveness of a multidisciplinary fall prevention program in community-dwelling elderly people: a randomized controlled trial (ISRCTN 647161113). *Intl J Technol Assess* 24(2):193–202
39. Robertson MC, Devlin N, Scuffham P, Gardner MM, Buchner DM, Campbell AJ (2001) Economic evaluation of a community based exercise programme to prevent falls. *J Epidemiol Community Health* 55:600–606
40. Kemmler W, Von Stengel S, Engelke K, Haberle L, Kalender WA (2010) Exercise effects on bone mineral density, falls, coronary risk factors, and health care costs in older women: the randomized controlled senior fitness and prevention (SEFIP) study. *Arch Intern Med* 170:179–185
41. Haines T, Hill A-M, Hill K, Brauer S, Hoffmann T, Etherton-Bear C, McPhail S (2013) Cost-effectiveness of patient education for the prevention of falls in hospital: economic evaluation from a randomized controlled trial. *BMC Med* 11:135
42. Campbell AJ, Robertson MC, La Grow S, Kerse NM, Sanderson GF, Jacobs RJ, Sharp DM, Hale LA (2005) Randomised controlled trial of prevention of falls in people aged ≥ 75 with severe visual impairment: the VIP trial. *BMJ* 331:817
43. Davis J, Marra C, Robertson M, Khan K, Najafzadeh M, Ashe M, Liu-Ambrose T (2011) Economic evaluation of dose-response resistance training in older women: a cost-effectiveness and cost-utility analysis. *Osteoporos Int* 22:1355–1366
44. Corrieri S, Heider D, Riedel-Heller S, Matschinger H, König H (2011) Cost-effectiveness of fall prevention programs based on home visits for seniors aged over 65 years: a systematic review. *Int Psychogeriatr* 23(5):711–723
45. Karinkanta S, Kannus P, Uusi-Rasi K, Heinonen A, Sievänen H (2015) Combined resistance and balance-jumping exercise reduces older women's injurious falls and fractures: 5-year follow-up study. *Age Ageing*. doi:10.1093/ageing/afv064